REMARKS

A. The Status of the Claims and the Amendments

Claims 12 and 14 have been amended. Claims 20 and 25 have been canceled without prejudice. Claims 1-11, 13, 15, and 19 have been withdrawn from consideration. Accordingly, claims 12, 14, 16-18, 21, and 22-24 are currently under consideration. The claims amendments clarify the language of the claims and harmonize the language of the claims with the specification.

In particular, with respect to the ligand X, the limitation of each of claim 12 and claim 14

> "X is a ligand selected from a group consisting of biotin, deiminobiotin, dethiobiotin, 1,2-dihydroxyethane, 1,2-dihydroxycyclohexane, digoxigenin, maltose, oligohistidine, glutathione, 2,4-dinitrobenzene, phenylarsenate, ssDNA, dsDNA, a peptide of polypeptide, a metal chelate, a saccharide, rhodamine, and hapten"

is disclosed in paragraph [0088] of the originally filed specification (pages 21-22).

With respect to the moiety R, the limitation of each of claim 12 and claim 14

> "R is selected from a group consisting of alkyl, pyridyl, substituted pyridyl, imidazole, pyrrole, thiophene, furan, azole, oxazole, aziridine, aryl, substituted aryl, amino acid, peptidyl, oligonucleotide and carbohydrate group"

is disclosed in paragraph [0086] of the originally filed specification (page 21).

Accordingly, it is submitted that the claims amendments do not introduce any new matter.

B. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 12, 14, 16-18, and 20-24 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention (the written description requirement). The claims have been also rejected as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (the enablement requirement).

The legal standard for determining both the adequacy of written description and the enablement was stated by the Applicants in the previous communication regarding this matter, and is incorporated herein in its entirety. The Applicants respectfully submit that the written description in this application satisfies the legal requirements and adequately supports the claims as amended. The Applicants also respectfully submit that the specification provides requisite enablement. The rejection is therefore respectfully traversed.

1. The Examiner has asserted again that there are no "distinguishing structural attributes" for the moieties "X" and "R." Claims 12 and 14 has been amended and now recite a number of "X" and "R" groups and provide precise chemical structures for each such group. Therefore, the specification describes the compound, R* (F – L) – X, which provides the structural relationship between the various groups in the molecule of the compound, and describes what those groups are. It is submitted that the compound to be used in the methods of the present invention is described adequately.

2. Second, the Examiner refers to a "wish list" of "potential compounds" again emphasizing that only one working example of a non-directed library of ABPs has been provided. For clarification, the Applicants point out that not one but several examples have been provided. More importantly, that the number of examples is generally

irrelevant. The Applicants are unaware of any controlling legal authority requiring that even a single "working" example be provided, and the Examiner provided no case or statutory requirement to that effect. Surely, the Examiner would agree that no examples at all need be present, since actual reduction to practice is never required. If this were not true, prophetic examples would not be allowed and could be labeled, using the Examiner's language, as a "mere wish list." Yet, the prophetic examples are very common, are not considered defective or insufficient, and are completely acceptable. It is submitted that there exists only a quite nebulous distinction between prophetic examples that could have been provided and what the Examiner calls "a laundry list" of potential groups.

The Applicants respectfully submit that so long as an adequate description of a product is provided, and those having ordinary skill in the art will understand how to make or use the product that is the subject of the invention, the requirements of Section 112 are satisfied, and nothing more is ever needed.

Nonetheless, even though they did not have to do so, the Applicants did provide not just one but seven examples. For additional clarification, the Applicants repeat their previous point that those skilled in the art recognize that each probe will vary depending upon the target protein. Accordingly, it cannot be said that only one library is taught in the specification, because the ability to label proteins based on the activity is a true characteristic of a probe; therefore, a variety of libraries is implicitly described. Combining this implicit disclosure with the examples, with the information regarding selection of the target proteins, and with the information regarding the functional groups, is clearly sufficient to demonstrate possession of the claimed invention.

3. The Examiner has raised the issue concerning the Adam's article and stated that the article demonstrated that the Applicants were not in possession of the claimed invention. To this assertion, the Applicants respectfully respond as follows.

The Adam reference discusses using a non-directed chemical library for screening the proteome, with the particular emphasis on characterization of low abundance proteins which are difficult to analyze using other analytical techniques. The gist of the article is that characterization of the proteins is based on their properties such as reactivity rather than on their abundance.

To support his conclusion that the specification does not provide adequate description and enablement, the Examiner used the following language from the Adam reference:

> "the discovery that the sulfonate probes non only labeled cALDH-I in complex proteomes but also inhibited this enzyme's catalytic activity suggests that, at least in this one example, a screen ... identified a small molecule-protein reaction that impacted the protein's ... function. If this correlation proves generalizable, non-directed approaches ... may generate chemical reagents applicable for both proteomics ... and cell based functional screenings."

The Examiner has stated that the language "at least in this one example" and "if this correlation proves generalizable" serves as "admission" that the Applicants were not in possession of the claimed invention. It is a mistake to link the Adam's article with this application.

First, the Applicants direct the Examiner's attention that the authorship of the article (Adam, Cravatt, Sorensen) is different from the inventive entity comprising the Applicants (i.e., Cravatt, Sorensen, Petricelli and Adam). Petricelli is not an author of the Adam's article and whatever was or was not "admitted" in the article is not binding on Petricelli, and accordingly, on the inventive entity as a whole.

Second, the expression "at least in this one example" does not show at all whether the authors discuss the only example available to them as the Examiner seems to have

concluded. Such conclusion is speculative. They may have additional examples or they may not and the Examiner does not have the definite answer to that. Is that not possible that the authors had other products in their possession but preferred to discuss this particular example and chose not to include other in the article? In this article, the authors concentrate on using biotinylated sulfonate esters for identification cALDH. The article is simply silent on what else the authors had or did not have in their possession. To infer from that silence that the inventors herein did not have anything else in their possession is illogical and unwarranted.

Third, the language "if this correlation proves generalizable" likewise does not show what the inventors had and did not have in their possession. The term "generalizable" is not defined in the article and the Examiner simply does not know what was really meant. Is it not possible that "generalizable" means "any compound whatsoever having the formula R* (F – L) – X" ? If so, the authors may not be in possession of every such compound, yet be in possession of every R* (F – L) – X having R, F, L, and X limited as in claims 12 and 14. The Examiner does not know the answer, therefore, cannot conclude the definite lack of possession.

The Applicants wish to remind that there is a strong presumption favoring finding of adequacy of written disclosure and enablement, as held by the precedent provided by the Applicants. It is respectfully submitted that the evidence provided by the Examiner is insufficient to rebut this presumption.

In view of the foregoing, the Applicants submit that the present specification contains a complete description of the invention sufficient to demonstrate that the Applicants, at the time the application was filed, had possession of the claimed invention and that the claims are enabled by that specification. Accordingly, it is respectfully submitted that the rejections of claims 12, 14, 16-18, 21 and 22-24 under 35 U.S.C. § 112, first paragraph, as allegedly lacking adequate written description, and as allegedly

lacking an enabling disclosure, are not properly applied. Reconsideration and withdrawal of the rejection are respectfully requested.

C. Rejection Under 35 U.S.C. 102(b)

Claims 12, 14, 16, 20, and 21 have been rejected under 35 U.S.C. 102(b), as allegedly being anticipated by Purohit et al. (*Biochemistry*, 1995, *34*, 11508-11514). Claims 12 and 14 recite using "a combinatorial chemical library comprising **a plurality of members** of the formula R* (F – L) – X".

As previously discussed, Purohit et al. fail to teach using a combinatorial chemical library which includes a plurality of compounds. The Examiner has stated that compounds (4)-(6) illustrated by Figure 1 on page 11508, Col. 2 in the Purohit et al. reference represent a combinatorial library. The Applicants respectfully disagree. There is nothing in Purohit et al. describing that compounds (4)-(6) can be used as a library, i.e., while being mixed together. Thus, a "plurality of members" limitation recited in each of claims 12 and 14 is not taught by Purohit et al. In addition, claims 12 and 14 recite a number of ligands X. None of these ligands can be found in Purohit et al. who only teach using estrone derivatives.

Accordingly, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. 102(b) are respectfully requested.

D. Rejection Under 35 U.S.C. § 103(a)

Claims 12, 14, 16-18, and 20-24 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Gygi et al. (*Nature Biotechnology* , 1999, 17(10):994-999), Liu et al. (*PNAS*, 1999, 96(26):14694-14699), and Bogyo et al. (*PNAS*, 1996, 94, 6629-6634). This rejection is respectfully traversed. None of the cited references, either alone or in combination, disclose or suggest the methods of the present invention.

With respect to claims 12 and 14, Gygi et al. fail to teach "a combinatorial chemical library comprising a plurality of members of the formula R* (F – L) – X" where "members of said combinatorial chemical library react with an active site of said protein member" recited in claims 12 and 14. Instead, as previously discussed, Gygi et al. treat two separate protein samples.

Further with respect to claim 12, Gygi et al. fail to teach that "inactivated complex mixture are comprised only of active proteins." Instead, the protein mixture described in Gygi includes only denatured proteins the activity of which have been destroyed. Gygi et al. teach that their "samples are combined and enzymatically cleaved" (page 994, left column, lines 18-19).

Accordingly, it is respectfully submitted that Gygi et al. does not disclose or suggest the methods of the present invention. Liu et al. and Bogyo et al., either individually, or in combination fail to cure the deficiencies of Gygi et al. Liu et al. only teach using fluorophosphonate-biotin for protein profiling. Bogyo et al. only teach using the probes with sulfonyl groups, such as probes derived from vinyl sulfones. There are no teachings in these references providing for the above-discussed elements of claims 12 and 14 that are missing from Gygi et al.

Additionally, the Applicants respectfully renew their previous argument that Liu et al. is not available as a prior art reference under 35 U.S.C. 103(a) since the subject matter set forth in Liu et al. was derived from the Applicants' own work. The Examiner rejected this argument based on the fact that the authorship of the Liu article represents a different inventive entity. The Applicants disagree again and would like to direct the Examiner's attention to MPEP § 716.10, Example 2, describing the situation identical to the situation in this case. Example 2 in MPEP § 716.10 shows that a 1.132 declaration, stating that the relevant parts of the reference originated with the applicants, is a proper tool for removing the reference.

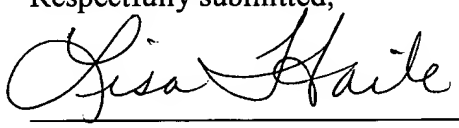
Consequently, claims 12 and 14 are shown to be patentably distinguishable over the cited art. Claims 16-18, 21 and 22-24 depend on claim 14 and are patentable for at least the same reasons. Accordingly, reconsideration and withdrawal of the rejection of claims 12, 14, 16-18, 21 and 22-24 are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Enclosed is a check in the amount of $860.00 for the Three (3) Month Extension of Time ($475.00) and Request for Continued Examination (RCE) ($385.00) fees. The Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayment, to Deposit Account No. 50-1355. A copy of the transmittal sheet is enclosed.

Respectfully submitted,



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